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Is impairment similar between arm and leg cranking exercise in COPD patients?☆

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Summary
Impaired skeletal muscle function has been reported in patients with chronic obstructive disease (COPD), but such impairment is not homogenous and its distribution between the upper and the lower limbs is still unclear. The present study was designed to assess and compare upper and lower limb capacities in patients with moderate to severe COPD during incremental and constant-load exercises. Thirteen COPD patients of similar age with moderate to severe air flow limitation (FEV_1: 35%±5% predicted) and 19 healthy subjects were studied. Four sessions were organized: two incremental and two constant-load cycling exercises with arm or leg in randomized order. As observed in a previous study involving incremental and constant tests, power, $\dot{V}O_2$, RER, $\dot{V}E$, and HR were all significantly lower in the upper and lower limbs of patients with COPD than in healthy controls. In the healthy population, aerobic capacity and mechanical efficiency (ME) were lower in the course of arm exercises than in leg exercises. For the same relative workload, dyspnea and blood lactate production were higher during arm exercise. In contrast, no significant difference was observed between arm and leg capacities for any of these parameters in COPD patients.

Abbreviations: BMI, body mass index; DH, dynamic lung hyperinflation; DLCO, carbon monoxide diffusion capacity; EELV, end expiratory lung volume; EILV, end inspiratory lung volume; fb, frequency of breathing; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HR, heart rate; IC, inspiratory capacity; $[la]_b$, blood lactate concentration; ME, mechanical efficiency; MVV, maximum voluntary ventilation; $PaCO_2$, arterial carbon dioxide pressure; PaO_2, arterial oxygen pressure; PMA, maximal aerobic power; REE, resting energy expenditure; RER, respiratory exchange ratio; RV, residual volume; SaO_2, oxygen saturation; TLC, total lung capacity; VAS, visual analogue scale; VC, vital capacity; $\dot{V}CO_2$, CO_2 excretion; $\dot{V}E$, minute ventilation; $\dot{V}O_2$, O_2 consumption; VT, tidal volume.

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Conclusion: Although aerobic capacity is impaired in COPD patients, arm aerobic capacity is relatively preserved. Given the lack of significant difference between arm and leg capacities in COPD, we hypothesize that upper limb muscles are less compromised than lower limb muscles in this patient population.

Introduction

Chronic obstructive disease (COPD) is one of the leading causes of both mortality and morbidity in developed countries.[1–4] It is now firmly established that this disease is associated with impaired skeletal muscle function.[5] Muscular deconditioning and genuine myopathy are the two main etiologies underlying this phenomenon.[6–8]

A muscle's oxidative and contractile capacities are enhanced by regular use which is the reason why patients with COPD are given pulmonary rehabilitation.[5] However, in such patients, some muscles are solicited even in the absence of any special reeducation program.

This is true of the diaphragm in which impaired function is partially reversed by the increased breathing effort even without reeducation.[9,10] Previous study reported that the functioning of the diaphragms of the patients with stable COPD was as good as in normal subjects at the same lung volume.[11] There is accumulating evidence that the diaphragm and other respiratory muscles are able to express adaptive changes in response to the chronic mechanical load imposed by the disease. This adaptation is accompanied by increased endurance and remodeling of the diaphragmatic muscle (increase in the number of mitochondria and changes in the types of muscle fibers produced).[12] We believe that the same applies to the muscles of the upper arm for three reasons: (i) in COPD, muscle strength and the muscle fiber profile of the upper extremities are better preserved than in the lower limbs[13–15]; (ii) quantification of physical activities in daily life in COPD reported that these patients reduce use of the lower limbs while use of the upper limbs remains relatively unchanged; and (iii) certain muscles of the scapular belt (the greater and smaller pectoral, greater rectus and anterior serratus muscles) mobilize the shoulder and also act as accessory respiratory muscles which are constantly solicited because of respiratory resistance (which is greater than in the healthy subject).[16]

We therefore hypothesize that, in patients with COPD, the aerobic capacity of upper limb muscles is better preserved than in the lower limb. To test this hypothesis, we intended to compare metabolic and respiratory adaptation in COPD during arm and leg pedaling exercises. Furthermore, we will focus on mechanical efficiency (ME) which reflects the conversion of chemical energy into mechanical energy.[17,18]

Methods

Subjects

Thirty five male subjects (mean age $\pm$ SD, 64 $\pm$ 6) divided into two groups were included in the study. Nineteen patients fulfilled the criteria of COPD according to the American Thoracic Society guidelines.[19] Among this group, 17 patients suffered from moderate IIb and two suffered from severe III COPD severity according to GOLD classification.[20] All patients were clinically stable with absence of respiratory exacerbation in the two months prior to the study. In the second group, 16 healthy men were recruited. The 10 control subjects were in good health with no history of lung disease, and with spirometry and lung volumes in the normal range. None of the control subjects engaged in regular physical training, with their average being less than 1 h per week. Informed consent was obtained from all subjects, and the Hospital Ethics Review Committee approved the study.

Measurements

Rest measurements

Subjects underwent pulmonary function testing in a hospital located at sea level (mean atmospheric pressure, 751 mmHg). During the first test, height and weight was measured and body mass index (BMI) (weight (kg)/height $(m)^2$) was calculated for each subject. Spirometry was performed using an automated metabolic measuring system (Oxycon pro, Jaeger, Würzburg, Germany), which was calibrated before each study with a known concentration of gas (i.e. 16% O_2 and 4% CO_2). Thoracic gas volumes were determined with a body plethysmograph (Masterlab, Jaeger, Würzburg, Germany). A mass flow sensor measured mouth flow, and volume was obtained by numerical integration of the flow signal. Partial and maximal flow–volume curves were obtained as follows: after at least four regular breaths, subjects forced expiration from end-tidal inspiration to residual volume (RV), which was immediately followed by a fast inspiration to total lung capacity (TLC) and a second forced expiration to residual volume (RV). All ventilatory parameters such as forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), maximum voluntary ventilation (MVV) and single-breath carbon monoxide diffusion capacity (DLCO) were obtained according to guidelines.[19,21–23] Resting energy expenditure (REE, expressed as an oxygen consumption per time unit) was measured during the patient's fasting state by indirect calorimetry using a ventilated hood system (Oxycon pro, Jaeger, Würzburg, Germany). Measurements were performed while the subjects were lying in a supine position for 30 min. At rest and on room air, arterial blood was drawn by radial artery puncture. Arterial oxygen pressure (PaO_2), carbon dioxide pressure ($PaCO_2$), oxygen saturation (SaO_2) and pH were measured by a Ciba Corning 855 gas analyzer (Ciba Corning Diagnostic, Medfield, MA).

Exercise measurements

All subjects completed four distinct exercises in this study. An incremental exercise was performed to assess physiological parameters at peak load exercise. A constant-load exercise (50% $\dot{V}O_{2max.}$) was used to determine ME, ventilatory and metabolic adaptations. Two sessions were both accomplished by the use of arm and leg cranking. In the first session, arm maximal exercises and leg maximal exercises were performed in a random order, and were separated by at least 1 week. In the second, arm constant load exercise and leg constant load maximal exercise were performed in a random order, and were separated by at least 2 days. Protocols used were identical during arm and leg exercises for both groups, and were performed on a Monark Ergomedic 818 (Varberg, Sweden) and a Monark compact rehab 871 E (Varberg, Sweden), respectively.

For arm exercises, the ergometer was lifted up to such a height that its cranks shaft was level with the shoulder of the subject, and the arms were alternatively stretched horizontally while cranking. Furthermore, the trunk was stabilized using two anatomic belts that fixed the subject's back to a stable support. Indeed, subjects could not use other muscles except those of arms and shoulders for arm exercises.

During all exercise tests, subjects breathed through a mouth-piece from which inspired and expired gas concentrations were continuously analyzed with a rapid response paramagnetic O_2 and infrared CO_2 analyzers, using a computerized breath-by-breath exercise system (Oxycon pro; Jaeger, Würzburg, Germany). Calibration measurements were carried out according to the manufacturer's instructions before each study. In all situations, before testing, ventilation characteristics were analyzed, at rest for 3 min.

Incremental cycle ergometry tests

After 1 min of unload cycling, power was increased by 10 W in the first 3 min, then increased constantly every second in order to have a rise of 6 W every minute until exhaustion. Cycling cadence was imposed at 60 revolutions/min^{-1}, which is considered the optimal energetic cadence.[24] Maximal workload was defined as the peak work exercise corresponding to the highest oxygen uptake value. In order to determine progressive air trapping and further dynamic lung hyperinflation (DH) during exercise, inspiratory capacity (IC), end expiratory lung volume (EELV) and end inspiratory lung volume (EILV) were measured as proposed by Hyatt.[25] DH was assessed only during the exhausted incremental exercise, at rest and at peak load exercise.

Severity of dyspnea was rated using the visual analogue scale (VAS) scoring between 0 (no dyspnea at all) and 10 (most severe sensation of dyspnea that the patient could imagine). Measurement of blood lactate concentration ($[la]_b$) enzymatic method (YSI 2300 Stat®, Yellow Springs Instruments, OH, USA), immediately after exercise.[26]

Constant-load exercise

All subjects performed, in a random order, 8-min leg exercise or arm exercise tests at 50% of individually measured peak work. Mean values recorded during the last two minutes of exercise were used for analyses. Mechanical efficiency was calculated from O_2 consumption and CO_2 production[24] from the following equation:

$$\begin{aligned} ME = &\text{ (power (W) of exercise} \\ &\times 0.01433 \text{ (kcal/min}^{-1}\text{)/(energy} \\ &\times \text{ expenditure during exercise} \\ &- \text{ REE) (kcal/min}^{-1}\text{)} \times 100\%. \end{aligned}$$

Statistical analysis

Data were expressed as mean ± SEM. The data distribution was analyzed before each test. Differences between patients and control subjects were compared using unpaired Student's *t*-test. In the event of cohorts of variables not having a normal distribution, the Mann–Whitney *U*-test was employed.

In each group, results of the arm and leg exercise protocols were also compared. When the data distribution reflected a normal distribution, we used a *t*-test for paired data. If the distribution was not normal, a non-parametric Wilcoxon test for paired data was employed.

Differences between groups were considered significant at $P<0.05$.

Results

Subjects

In our study, patients in the COPD group had moderate to severe airflow obstruction (FEV_1 of 35 ± 5% predicted normal values). Mean anthropometric and resting data for the COPD patients and control group are presented in Table 1. No significant differences in age, height, weight or BMI were observed between the two groups.

Incremental cycling exercise

All results are presented in Table 2.

At peak exercise, maximal values of power, $\dot{V}O_2$, RER, $\dot{V}E$, and HR were significantly lower in patients with COPD, compared with healthy controls for both conditions. The lower ventilation in COPD patients, compared with healthy controls, was related to a significantly smaller tidal volume and lower breathing frequency. In the COPD group, for both conditions, the peak ventilation (expressed as a percentage of predicted maximal voluntary ventilation) was significantly higher than in the control group.

In the control group, maximal values of power output, $\dot{V}O_2$ and $\dot{V}E$ were significantly lower during arm than leg cycling (mean difference for $\dot{V}O_2$ and $\dot{V}E$, −27.8% and −20%, respectively; $P<0.05$). However, blood lactate concentration and the dyspnea scale were higher during arm exercise ($P<0.05$). We have observed an alteration in maximal power output corresponding, respectively, to 57% for leg and 35% for arm in COPD group when compared with healthy subjects ($P<0.05$).

Dynamic hyperinflation (DH)

At rest and at peak exercise, no DH was observed among the control subjects. In contrast, for COPD patients at rest and peak exercise, in both conditions (arm and leg cranking), we noted a DH ($P<0.05$). Furthermore, in this group no difference in DH values was observed between rest and peak exercise of either arms or legs (Fig. 1).

Table 1 Characteristics of subjects at rest.

	COPD ($n=16$)	Control ($n=19$)
Age (yrs)	65±6.1	63±5.3
Height (m)	165±12	169±8.4
Weight (kg)	75±13	79±10
BMI (kg m^{-2})	23.5±6.3	27.36±5.8
VC (L)	1.97±0.64*	3.99±1.12
(%predicted)	59±17*	101±6
FEV_1 (L)	0.932±0.25*	2.97±0.98
(%predicted)	35±5*	102±4
FEF 25–75 (L)	2.336±0.873*	3.68±1.09
(%predicted)	18±3*	88±15
FEV_1/FVC (%)	48±5.28*	75±5
RV (L)	4.82±1.25	–
(%predicted)	221±69	–
DLCO (ml min^{-1} mmHg^{-1})	11.8±6.2	–
(%predicted)	62±18	–
SaO_2 (%)	95±1.8	98±1
PaO_2 (mmHg)	74±3.25	–
$PaCO_2$ (mmHg)	40±1.35	–
Arterial pH	7.41±0.08	–

Values are means±SE. COPD, chronic obstructive pulmonary disease; *n*, no. of subjects; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; RV, residual volume; DLCO, CO diffusion capacity; SaO_2, oxygen saturation; PaO_2, arterial oxygen pressure; $PaCO_2$, arterial carbon dioxide pressure; *$P<0.05$.

Constant-load exercise

Parameters recorded during constant load exercise are presented in Table 3.

In the COPD group, for both exercises, mean values of power, $\dot{V}O_2$, $\dot{V}E$, and HR were significantly lower than in the control group. Furthermore, the lower ventilation values in the COPD group reflected a significantly smaller tidal volume and a significantly lower breathing frequency. For both exercises, the ventilation expressed as a percentage of predicted maximal voluntary ventilation was similar in patients with COPD (but significantly higher compared to controls). In the COPD group, there was no significant difference in power, $\dot{V}O_2$, RER, $\dot{V}E$, HR, ME and blood lactate concentration between leg and arm exercise.

In the control group, values of $\dot{V}O_2$, $\dot{V}E$, and HR were significantly lower during arm exercise than during leg exercise.

During arm exercise no significant difference was observed in ME between COPD patients and control group (respectively, 20.97%±2.33% vs. 25.90%±3.30%). In contrast, during leg exercise, ME was significantly lower in the COPD group than in the control group (respectively, 20.91%±2.92% vs. 27.38%±3.03%, $P<0.05$) (Fig. 2).

Discussion

The most striking result of the study was the relatively diminished impairment during arm than leg exercise, giving rise to an identical aerobic capacity in arm and leg in moderate to severe COPD patients.

Impaired aerobic capacity in COPD and the reason of this dysfunction is now well documented.[5] Our results are in agreement with this observation since our patients with moderate to severe COPD ($FEV_1<40\%$ predicted) compared with healthy subjects. During constant-load exercise, muscle functions are usually assessed by measurement of ME.[17,18] As the ME of locomotion corresponds to the efficiency of conversion of chemical energy to kinetic energy by muscle,[24] an alteration in muscle function leads

Table 2 Peak arm and leg exercise responses for both groups.

	Arm crank		Leg cycle	
	Controls	COPD	Controls	COPD
Max. *W*, W	94±12.65†	54±8.54*	162±21.50	58±10.33*
$\dot{V}O_2$, ml min^{-1}	1597±168†	1054±67*	2190±271	1109±116*
RER	1.15±0.04	1.09±0.03*	1.14±0.05	1.08±0.03*
$\dot{V}E$, l min^{-1}	61.8±6.2†	28.9±3.21*	77.2±9.53	31.6±4.06*
$\dot{V}E$/MVV, %	60.2±4.8†	88.6±1.6*	74.9±5.8	95±2.1*
V_T, l	1.64±0.13†	0.92±0.18*	1.95±0.23	0.98±0.17*
f_b, breaths min^{-1}	37.8±2.9†	31.5±3.4*	39.8±3.34	32.5±3.3*
Dyspnea scale	6.7±1.5†	8.1±1.2*	7.5±1.3	8.9±1.1*
HR, beats min^{-1}	156±5.7	117±6*	157±5.1	125±8.8*
Lactate, mol ml^{-1}	8.8±1.4	4.1±0.7*	7.2±1.2†	4.3±0.9*

Values are means±SE; $\dot{V}O_2$, O_2 consumption; $\dot{V}CO_2$, CO_2 excretion; RER, respiratory exchange ratio; $\dot{V}E$, minute ventilation; MVV, maximal voluntary ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate; $^{\dagger}P<0.05$ arm vs. leg; *$P<0.05$ COPD patients vs. control.

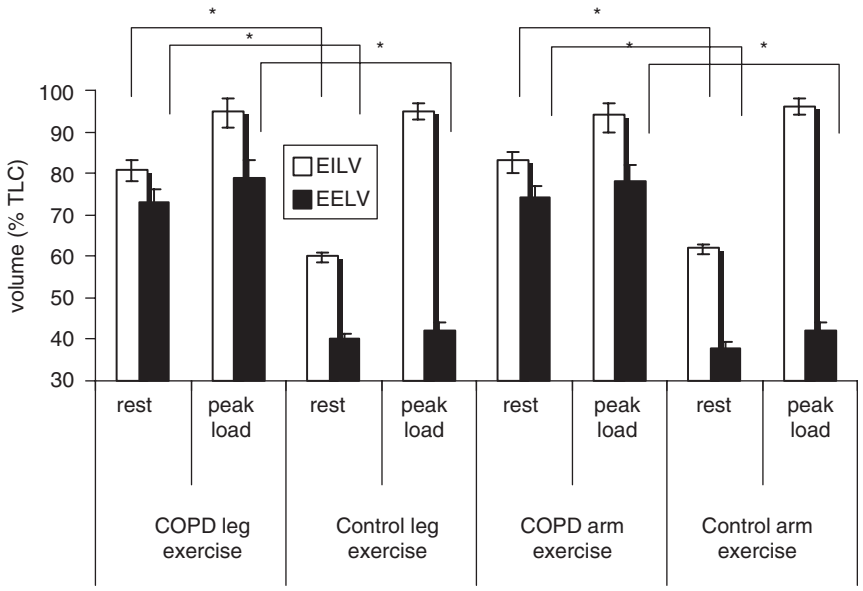

Figure 1 Dynamic hyperinflation (DH) assessment in COPD patients and healthy subjects. Subdivisions of lung volume, expressed as percentage of total lung capacity (TLC) at rest and at peak work exercise during both arm and leg exercise in controls and in patients with COPD. *$P<0.05$ leg EILV patients vs. control; *$P<0.05$.

Table 3 Physiological parameters recorded at 50% peak aerobic capacity.

	Arm crank		Leg cycle	
	Controls	COPD	Controls	COPD
50% peak work				
$\dot{V}O_2$, ml min^{-1}	898±76†	724±37*	1257±123	778±81*
RER	0.94±0.01	0.98±0.02*	0.93±0.02	0.97±0.03*
$\dot{V}E$, l min^{-1}	26.1±3.8†	21.2±3.5*	28.2±3.7	22.5±2.3*
$\dot{V}E$/MVV, %	25±2.1	67.7±5.3*	27±3.6	71.4±3.2*
V_T, L	1.21±0.21	0.827±0.16*	1.29±0.20	0.854±0.19*
f_b, breaths min^{-1}	21.4±2.8	25.9±3.5*	21.9±2.3	27.1±3.6*
HR, beats min^{-1}	93±11.8†	92±4.6	108±6.8	96±8.4*
Lactate, mol ml^{-1}	3.7±0.7†	1.8±0.3*	2.7±0.5	1.9±0.4*

Values are means±SE; $\dot{V}O_2$, O_2 consumption; $\dot{V}CO_2$, CO_2 excretion; RER, respiratory exchange ratio; $\dot{V}E$, minute ventilation; MVV, maximal voluntary ventilation; V_T, tidal volume; f_b, frequency of breathing; HR, heart rate; $^{\dagger}P<0.05$ arm vs. leg; *$P<0.05$ COPD patients vs. control.

to an impairment in efficiency. In our study, the ME of leg cycling was lower in patients with COPD than in controls, indicating that the skeletal muscle function was altered at least in lower limb muscle in our COPD patients.

In healthy subjects, when comparing arm and leg capacities during maximal exercise, it is reported that peak arm power, peak arm $\dot{V}O_2$ and peak arm $\dot{V}E$ are significantly lower when compared to peak leg values.[16] Our results can be compared with these previous observations. In the healthy population, this result is explained by a lower muscle mass in the arms and by the existence of ventilatory limitation during arm activities. During arm exercise, some accessory respiratory muscles, contributing to inspiration with a fixed extra thoracic anchoring point, are used for arm crank cycling and may thus impair breathing efficiency.[27,28]

Surprisingly, no difference between arm and leg aerobic capacity was observed in patients with COPD. This suggests a higher muscular dysfunction in lower limb muscle compared to upper limb. Furthermore, at an relative equivalent workload, there was no statistic difference in ME during arm exercises between COPD and healthy subjects, whereas the ME of leg cycling was significantly lower in patients with COPD than in healthy subjects ($P<0.05$). This observation confirms that leg muscles are more profoundly affected than arm muscles in terms of aerobic capacity.

In order to confirm that the differential aerobic capacity between the upper and lower limbs is indeed secondary to impaired muscle function, we plan to analyze the ''out-of-breath'' feeling induced by each of these two types of exercise. In healthy subjects, for an identical relative

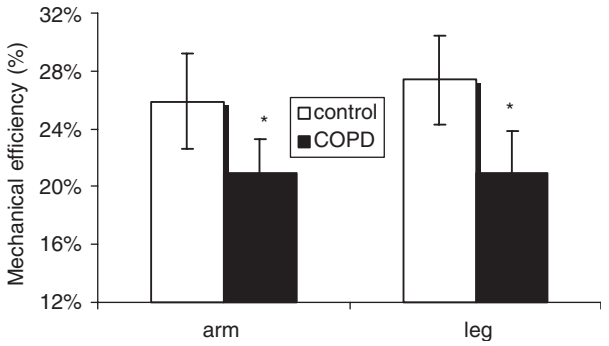

Figure 2 Mechanical efficiency (ME) in COPD patients and in healthy subjects. Bar diagram of leg and arm mechanical efficiencies in COPD patients (darkened bars) and healthy subjects (light bars). Mean values ± SEM are shown. Significance of differences was indicated as $*P < 0.05$ for COPD patients vs. healthy subjects.

workload, the ''out-of-breath'' feeling is augmented further during arm exercise than during leg exercise.[27] Among patients with COPD, we observed no significant difference between the dyspnea associated with peak arm and leg exercises.

It is accepted that exercising patients with COPD become out-of-breath for two reasons: (i) ventilatory, notably due to DH, and (ii) metabolic, as a result of increased lactate production, in which metabolism is predominantly glycolytic. In our study, impaired ventilatory function cannot account for why the impression of being dyspneic is the same regardless of whether the exercise involves the arms or the legs. In practice, in COPD, we observed no significant difference in ventilatory parameters ($\dot{V}E$, Fb and especially DH) during arm as opposed to leg exercise. In the light of these findings, we do not believe that ventilatory limitations in COPD can account for the ''relatively greater degree of dyspnea'' observed in the course of leg as opposed to arm exercise.

Previous studies have suggested that, for the same power output, arm exercise requires higher oxygen uptake, carbon dioxide output, and ventilation than leg exercise, and that response kinetics are slower.[29] On the other hand, it is accepted that, in healthy subjects performing arm exercises, the venous blood lactate concentration is significantly higher than during leg exercise.[30] Several reasons are proposed to explain this situation, yet the most prominent is that upper limb muscle fiber typology is more glycolytic than lower limb muscle fibers. In healthy subjects, our findings are consistent with previous results of the literature (with a significantly lower blood lactate concentration during leg exercises when compared with arm exercises, $P < 0.05$). Conversely, in subjects with COPD, no significant difference in blood lactate concentration was observed between arm and leg values, in either peak or constant-load exercises. Thus, in COPD, the lack of any difference between ventilatory parameters between arm and leg could be mainly due to a metabolic difference in the upper and lower limbs than to an impaired ventilatory function.

The main result of our study is that in moderate to severe COPD patients, upper and lower limbs have a similar aerobic capacity with a comparable DH. This observation suggests less arm muscle dysfunction in COPD. One possibility is that a part of the upper limb mass muscle is relatively less deconditioned compared to the lower limb in COPD patients, accounting for the relatively preserved values of maximal workload during arm exercise. In this respect, studies of skeletal muscle function in COPD have demonstrated that upper limb muscles were less affected than lower limb muscles.[13,14,31] Thus, the reduction in quadriceps strength averaged 30% when compared with healthy subjects[14,32,33] whereas upper limb strength was relatively preserved compared with the lower limbs.[31] Furthermore, Sato et al.[15] noted that muscular fiber typologies in brachial biceps were similar to those of healthy subjects. One factor that may explain these observations is the fact that in COPD, shoulder girdle muscles such as the pectoralis major and minor, latissimus dorsi, and serratus are regularly active during quiet breathing, whereas these muscles are generally not used during breathing in healthy subjects.[30] It may be that muscles used both for breathing and arm exercises are relatively less deconditioned than leg muscles in COPD patients. This phenomenon has also been observed in the diaphragm: in COPD, impaired function in this muscle is partially compensated by an increase in its workload.[12]

In summary, this study indicated that, in patients with moderate to severe COPD, despite a significant alteration in muscular function, there was relatively little difference between upper and lower limb aerobic capacity compared with healthy individuals. COPD patients may have a tendency to eliminate lower limb activities involving the muscles of ambulation, leading to an overall deconditioning. In our point of view, differences between upper and lower limb muscle capacities need to be evaluated in patients with severe to moderate COPD, in order to design suitable training and rehabilitation procedures.

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